Supporting Information

Astrocyte-Targeted Transporter-Utilizing Derivatives of Ferulic Acid Can Have Multifunctional Effects Ameliorating Neuroinflammation and Oxidative Stress in the Brain

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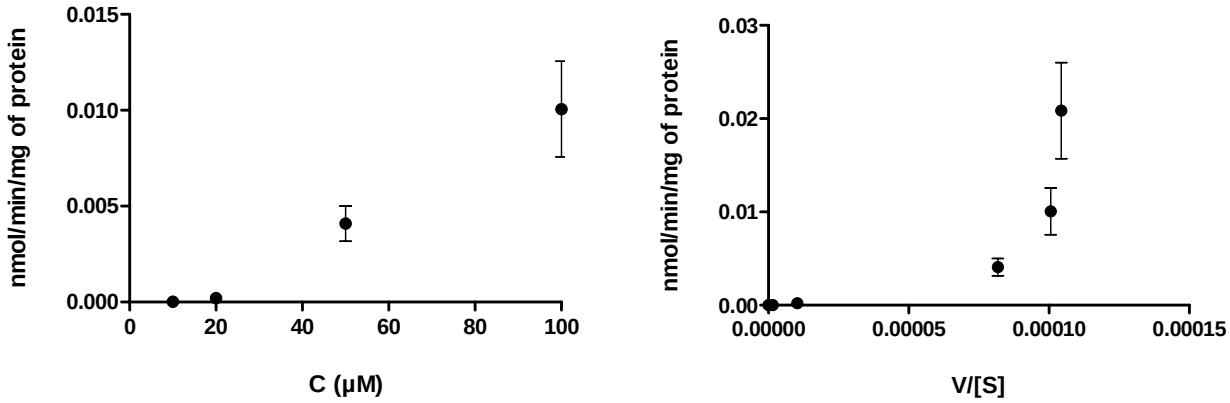
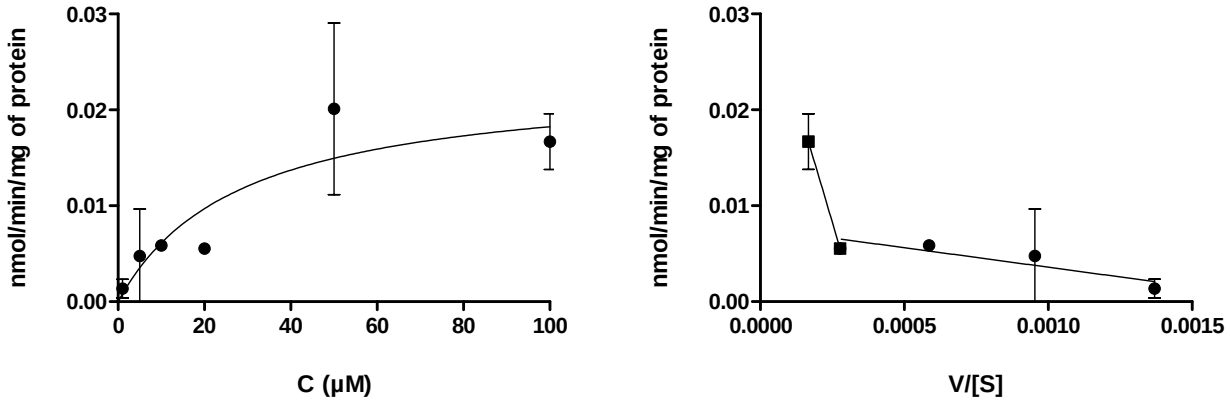
1. Uptake of Ferulic Acid and Its LAT1-Utilizing Derivatives into Astrocytes via LAT1

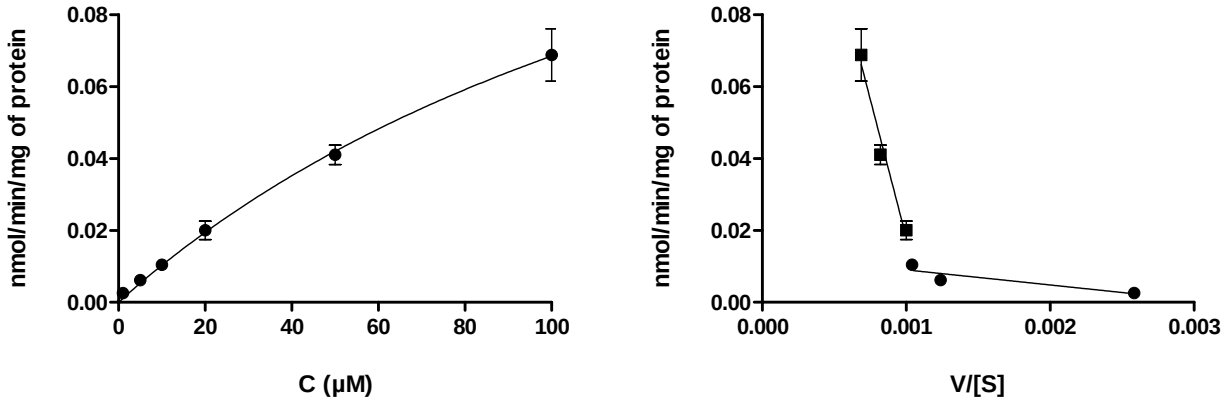
A) Ferulic Acid (FA)



B) Derivative 1



C) Derivative 2



D) Derivative 3

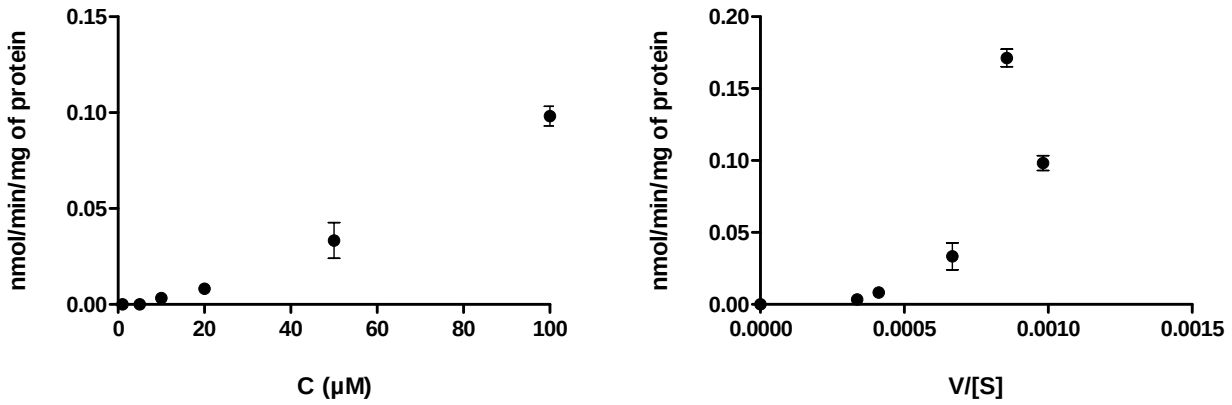


Figure S1. Cellular uptake of ferulic acid (**A**) and its LAT1-utilizing derivatives (**1-3; B-C**) into primary astrocytes over a concentration range 1-100 µM (left) and the Eadie-Hofstee plots for transporter-mediated uptake mechanisms (right). The data is presented as mean ± SD (n=3).

2. Intracellular Unbound Concentrations of Ferulic Acid and Its LAT1-Utilizing Derivatives

Table S1. Unbound Fraction, $f_{u,cell}$ (%) of FA And Its LAT1-Utilizing Derivatives **1-3**. The data is presented as mean ± SD (n=3).

Compound	**$f_{u,cell}$ (%)**
FA	*Fully unbound*
FA-Derivative 1	16.26 ± 2.72
FA-Derivative 2	8.06 ± 0.54
FA-Derivative 3	*Cannot be evaluated due to the metabolism*

3. Ability of Ferulic Acid and Its LAT1-Utilizing Derivatives to Inhibit Astrocyte Cell Growth

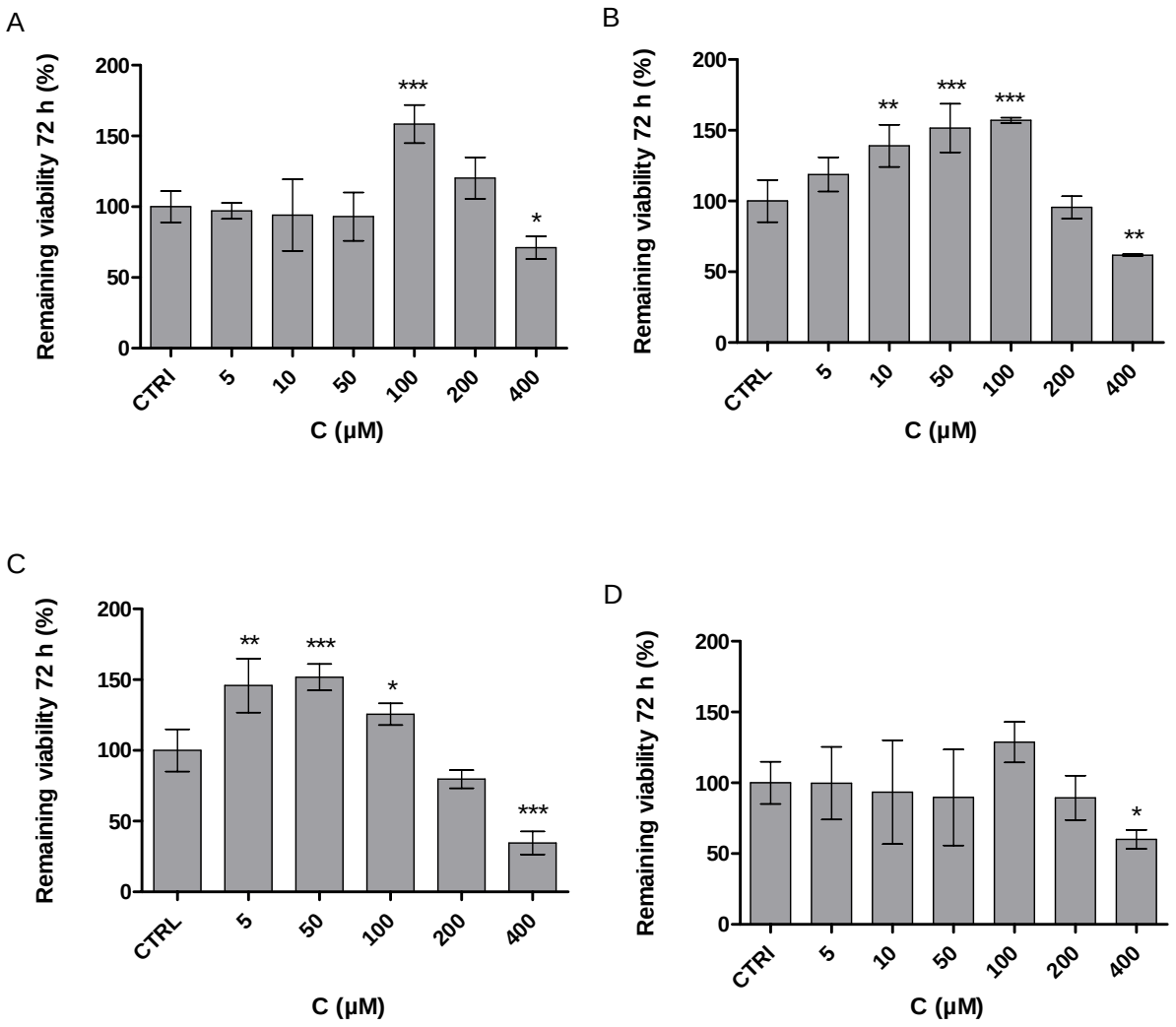


Figure S2. The remaining cell viability of primary astrocytes after 72 h incubation of 1-400 µM ferulic acid (**A**) and its LAT1-utilizing derivatives **1** (**B**), **2** (**C**) and **3** (**D**) presented as percentages (%) compared to the untreated cells (ctrl) (mean ± SD, n=3-6). An asterisk denotes a statistically significant difference from the respective control (*** $P < 0.001$, one-way ANOVA, followed by Tukey's test).

4. Ability of Ferulic Acid and Its LAT1-Utilizing Derivatives to Inhibit AChE/BuChE Activity

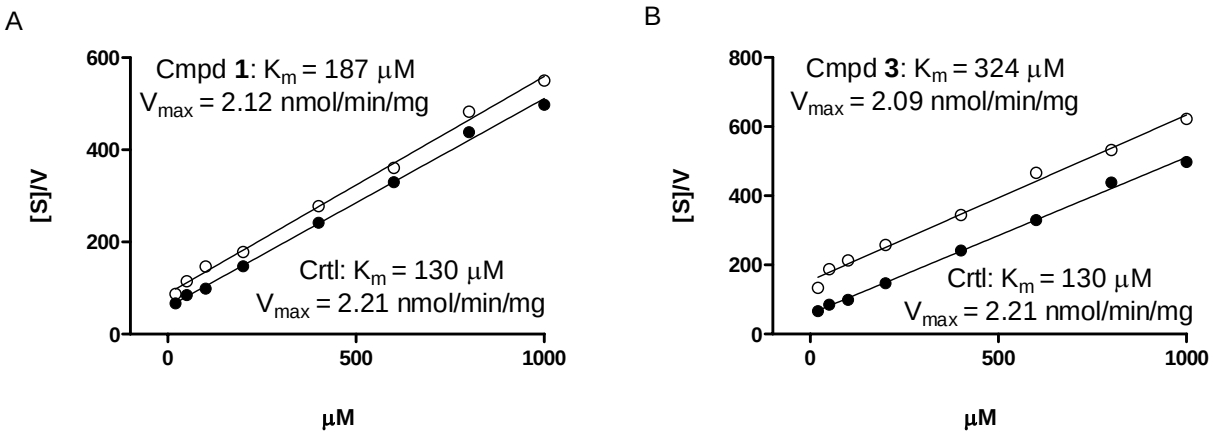


Figure S3. Hanes-Woolf's plots of AChE activity in the presense of 16-66 µM FA-derivatives **1** and **3** (**A**-**B**, respectively; open circles) compared to the control (filled circles).